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(71) Applicant *(for all designated States except US)*: **BIO-QUELL MEDICAL LIMITED** [GB/GB]; 30-31 Lynx Crescent, Weston-Super-Mare, Somerset BS24 9BP (GB).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **GUESS, Roger** [GB/GB]; 14 The Boundaries, Lympsham, Somerset BS24 0DF (GB).

(74) Agent: **BOULT WADE TENNANT**; Verulam Gardens, 70 Gray's Inn Road, LONDON WC1X 8BT (GB).

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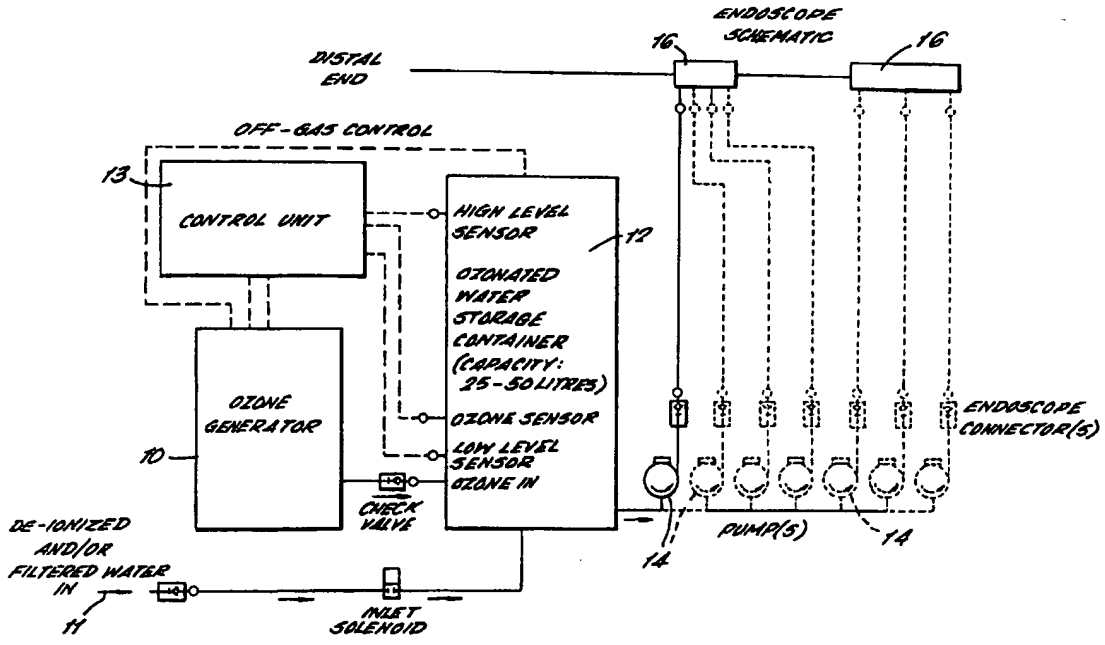
(54) Title: DECONTAMINATION OF MEDICAL EQUIPMENT



(57) Abstract: An apparatus for cleaning medical equipment comprising a supply (11) of filtered water, a supply (12) of ozonated water containing a predetermined concentration of water and means (14) for delivering first a flow of filtered water over the surfaces of the equipment to be cleaned for a predetermined time followed by a flow of ozonated water over said surfaces for a predetermined time to disinfect the surfaces.

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PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

DECONTAMINATION OF MEDICAL EQUIPMENT

This invention relates to the decontamination or disinfection of medical equipment such as endoscopes and other healthcare equipment including bedpans.

Medical devices and in particular endoscopes have historically been disinfected by either heat or chemicals. Current disinfection of endoscopes is carried out by two methods; one a cold process, and the other a heated process.

i) **Cold Process**

This is normally used when the endoscopes cannot be disinfected by using heat, i.e. most flexible endoscopes. The endoscopes are manually cleaned and then put into a washer disinfector for an automatic process. This process gives the scopes a pre-wash, a wash with a disinfectant, and a final rinse with water. The disinfectant wash allows a contact time dependent on the manufacturer of the disinfectant, e.g. Cidex (Johnson and Johnson), Nu-Cidex (Johnson and Johnson), Gigasept (Schule and Mayer).

Cold processing allows a batch of disinfectant to be re-used, the number of cycles dependent on the washer disinfector and the level of dilution taking place. Once this number of cycles is completed, the batch of disinfectant is dumped to waste and the machine re-charged with a fresh bash.

ii) **Hot Process**

Some endoscopes (mainly rigid ones) can be processed in a normal sterilising autoclave

at 120-130°C. For endoscopes such as flexible ones that cannot withstand this temperature, there are a range of washer disinfectors that disinfect by heating to a lower temperature of 50-55°C.

This process gives the scopes a pre-wash, a heated wash with a small amount of disinfectant, and then a final rinse with water. The heated wash takes a small amount of concentrated disinfectant, and by heating to 50-55°C causes the chemical to vaporise and thus provide the efficiency required. This process normally uses gluteraldehyde as the disinfectant, and the small amount used each time is a single use. This process tends to have longer cycle times than cold processing.

The heated process is more prevalent in Europe, while cold processing is utilised in the UK and US.

The method of the invention also provides an alternative to the use of steam.

Ozonated water is widely used to kill bacteria. However, when generating and dissolving ozone in water it is usual to expect levels of under 1 ppm. We have found that we are not able to disinfect medical devices to the required standard or within an acceptable time period using such levels of ozone concentration. Effective disinfection can only be achieved with a precise combination of flow over and through the device, ozone levels, and time.

The criteria for disinfection of the endoscopes have been developed by Dr. J Babb of the Hospital Infection Research Laboratory (HIRL) at City Hospital

NHS Trust, Birmingham, as described later and is key to the validation of the process. The process fulfils the HIRL test criteria for endoscope washer disinfectors, i.e. mean $\log_{10}$ reduction >6 (99.9999%) with no individual reduction <5 (see Appendix 3). Although external validation of the process can be undertaken, it is impractical to undertake on a daily basis. Within the process we have been able to measure the ozone levels at the inlet and outlet of the process. This has allowed us to calculate how long the process needs to run to give the required disinfection. As ozone concentration is depleted on contact with bacteria, if the inlet and outlet levels are identical there is minimal bacteria remaining. As bacteria levels have to be very low to validate the unit for a predetermined time after equilibrium is reached.

Thus this invention relates to ozonated water as a substitute for the traditional chemical method of disinfection. Although the development and validation has been undertaken on endoscopes, the process and technology is relevant to many medical devices.

This invention provides a method of cleaning medical equipment comprising the steps of flowing filtered water over surfaces of the equipment to be cleaned for a predetermined time followed by flowing ozonated water containing a predetermined concentration of ozone over said surfaces of the equipment for a predetermined time to disinfect the surfaces.

Preferably the ozonated water is de-ionized prior to ozonating to the predetermined concentration.

In one method according to the invention the de-ionized water is obtained from a supply of de-ionized water.

Alternatively the water is de-ionized by ozonating the water to remove free ions in the water

following which ozone is added to the predetermined concentration.

In any of the above methods a surfactant is added to the ozonated water and the predetermined concentration of the water is reduced to a selected lower level.

Also in any of the above methods the flow of filtered water may be obtained from tap water.

In the case where the medical equipment has internal throughways and external surfaces to be cleaned, said filtered water and ozonated water may be caused to flow through the internal surfaces and are flowed or sprayed on the external surfaces to disinfect the external surfaces.

The invention also provides an apparatus for cleaning medical equipment comprising a supply of filtered water, a supply of ozonated water containing a predetermined concentration of water and means for delivering first a flow of filtered water over the surfaces of the equipment to be cleaned for a predetermined time followed by a flow of ozonated water over said surfaces for a predetermined time to disinfect the surfaces

The following is a description of some specific embodiments of the invention, reference being made to the accompanying drawings in which:

Figure 1 is a schematic diagram showing an apparatus for carrying out decontamination of medical equipment such as endoscopes;

Figure 2 is a more detailed view of an apparatus for producing ozone gas using a proton exchange membrane cell;

Figure 3 is a more detailed view of the proton exchange membrane cell of Figure 2;

Figure 4 is a diagrammatic illustration of the key factors in controlling the decontamination process; and

Figures 5 to 9 are graphical illustrations plotting log kill of bacteria against the concentration of ozone in the ozonated water in parts per million for different water/de-ionized water/filtered water and surfactant combinations.

Figure 1 shows a unit based around an electrochemical generator stack 10, where Hydrogen (H) and Ozone (O^3) are generated. The stack is fed by a dedicated de-ionised water supply 11 at a pressure of one bar, to maintain the integrity and efficiency of the cells and the long-term quality of the feed water. Power for the stack is supplied from a variable DC supply (not shown). There is also a battery back-up system (not shown) to support the cell in the event of a power failure. Hydrogen gas is re-absorbed and/or catalytically converted.

Figure 2 shows a proton exchange membrane ozone generation system and Figure 3 shows the ozone generation cell in more detail.

Ozone is supplied under pressure to a contactor 12 containing 25-50 litres of filtered water via a diffuser block. This allows the ozone gas to bubble into the water to produce a high concentration solution (typically at least 4 ppm, for example 6+ppm and possibly up to 15ppm). The level of water in the contactor is controlled and filled through solenoid valves, the operations being initiated by a micro-processor operated control unit 13 through software instructions. Ozone concentration levels are constantly monitored to ensure correct values.

Any excess ozone off-gas is collected at the top of the contactor and passed to a destruct column, where it is processed through an absorber. When operating at full capacity the cell produces perceptible heat, and so water used in the cell for electrolysing is cooled with a heat exchanger and refrigeration plant.

Cycle

The initial work allowed us to achieve a log 6 kill (i.e. disinfection). We have developed the process by utilising the mechanical removal of the water flow (at 2.2l/min) initially with unozonated water, followed by ozonated water. This minimises the requirement for ozonated water and thus the size of the ozone generator. A number of trials were undertaken and an optimised cycle was developed of 10 minutes unozonated water and 6 minutes ozonated water. With this cycle and work on the water quality we have achieved a high level disinfection (i.e. log 9 or total kill on Pseudonomas aeruginosa). This work also indicated that 15ppm was important.

Water Quality

We have undertaken a number of trials to establish if water quality could adversely effect or improve the kill. We believed that de-ionised water would put less burden on the ozonated water and therefore make the ozonated water more effective. Four different water qualities were considered:

a) de-ionised filtered water;

b) filtered tap water;

c) de-ionised filtered ozonated water;

d) filtered ozonated tap water.

What we found was that:

a) it is unimportant what quality of water is used in the initial rinse section of the process;

b) if de-ionised water is used rather than tap water for the final ozonated water section the results will be improved;

c) if the tap water is ozonated for a prolonged period prior to being used it can be made to react in a similar way to de-ionised water. This is a variation on b).

Surfactant Use

Recent work has indicated that we can get very good results by adding a small amount of Fairy Liquid (the surfactant) into the ozonated water.

We have run a short cycle (6 minutes unozonated + 6 minutes ozonated) at a much reduced ozone level (5ppm). In both tests when using a surfactant in the ozonated water the kill was total. In one of the two tests injecting in the rinse water, the kill was total.

To disinfect effectively an endoscope, ozonated water needs to be pumped through all the internal channels of the scope at a flow rate and concentration level sufficient to kill organisms that may remain after a manual clean has taken place. The water is supplied at ambient temperature but could be pre-heated up to 40°C to accelerate the disinfection process if required. In our testing we have found these to be concentration level of at least 4ppm, preferably about 6ppm and not more than 15ppm, and a flow rate that equates to 2.2 l/min. These parameters need to be applied for a minimum period of 10 minutes and a maximum of 15 minutes to ensure all internal channels of a normal endoscope have been disinfected. In addition rinse water and ozonated water may also be flowed over the outer surface of the endoscopes to disinfect these as well.

Ozonated water is supplied from the contactor to a supply pump 14 having connectors 15 for coupling to the individual endoscope channels 16. Spent ozonated water is directed to waste via the distal end of the endoscope 19. Alternatively the spend ozonated water could be recirculated to the contactor for re-ozontation.

Kill Rate Optimisation Programme

Cycle combination of:

a) de-ionised water (DIFW)
b) filtered water (FW)
c) de-ionised filtered ozonated water (DIFOW)
d) filtered ozonated water (FOW)

Cycle:

1) 5 min DIFW + 6 min DIFOW
2) 5 min FW + 6 min FOW
3) 5 min DIFW + 10 min DIFOW
4) 5 min FW + 10 min FOW
5) 10 min DIFW + 6 min DIFOW
6) 10 min FW + 6 min FOW
7) 10 min DIFW + 10 min DIFOW
8) 10 min FW + 10 min FOW
9) 10 min FW + 10 min DIFOW
10) 10 min FW + 6 min DIFOW
11) 10 min FW + 10 min FOW (with 20 min delay)

Key factors:

a) di water required for ozonation;
b) 15ppm dissolved ozone required;
c) high water flow;
d) combination of flows.

Observations:

a) temperature not critical (up to 21°C);
b) water quality not critical.

Machine to only require water, electricity and drainage to operate.

Operator interface to be via touch screen.

Automatic setting of scope parameters scope by tagging reader system.

Machine to be totally PLC controlled with:

a) data storage of previous 500 cycles;
b) downloading facility to PC or Internet;
c) full monitoring system i.e. all cell voltages;
d) remote monitoring or fault finding down

telephone line;

e) multi-layer password protection.

Single pass system of liquids.

Rinse water will be tap water. Ozonated may be de-ionised.

May use vertical hanging of scopes.

Advantages of the PEM System

a) high concentration of ozone generated quickly (eg: 18% wt/wt - and higher)

b) small footprint for equipment

c) pure ozone generated (ie. no impurities)

Alternatively a common discharge technique may be used for creating the ozone supply in place of the ozone generator.

Electrochemical formation of ozone

Anodic reactions

$2H_2O \rightarrow O_2 + 4H^+ + 4e^-$; $E^\bullet = 1.23V$

$3H_2O \rightarrow O_3 + 6H^+ + 6e^-$; $E^\bullet = 1.51V$

Cathodic reactions

$2H^+ + 2e^- \rightarrow H_2$; $E^\bullet = 0.00V$

$O_2 + 4H^+ + 4e^- \rightarrow 2H_2O$; $E^\bullet = 1.23V$

Electrocatalysts

- high oxygen overpotential
- stable at high current densities
- stable in the presence of aggressive electrolytes
- high catalytic activity and selectivity

Latest results - log 8.5 kill from log 8.5 loading

Aqueous ozone preparation parameters

Water quality: de-ionised, filtered tap water

- pre-filtered to 1 µ
- standard de-ionisation to 3mS

Temperature of water: 14°C

Water pressure: 0.5 bar (7.4 psi)

Ozone concentration: 14 ppm

Flow rate: 2.2 $lmin^{-1}$ (through the endoscope lumens - ie internal irrigation channel)

Bio-burden reduction data

Test equipment: internal lumen of an Olympus Gastroscope GIF1K and Fujinon Gastroscope

Test organism: *pseudomanas aeruginosa* ATCC 9027 - log 8.5cfu loading

Log 8.5 reduction after c.15 minutes

➡ ***High level disinfection achieved***

Inoculation and disinfection protocol

Microbiological testing laboratory	:	MICROCHECK Technical Services (UKAS accredited microbiological testing laboratory)
Innoculum	:	*pseudomanas aeruginosa* (ATCC 9027) - 5.0 x 10^8cfu - and 10% horse serum as a soiling agent
Test method	:	draining / drying period of 10 minutes before sampling
	:	various cycles of water / ozone - flushed with 10-20mls of sterile water and collecting the washings and culturing the surviving organisms
Culture	:	medium: tryptone soya agar
	:	incubation: 37°C for 24 hours
Dilution	:	maximum recovery diluent
Quenching agent	:	Lecithin / Tween / Sodium thiosulphate

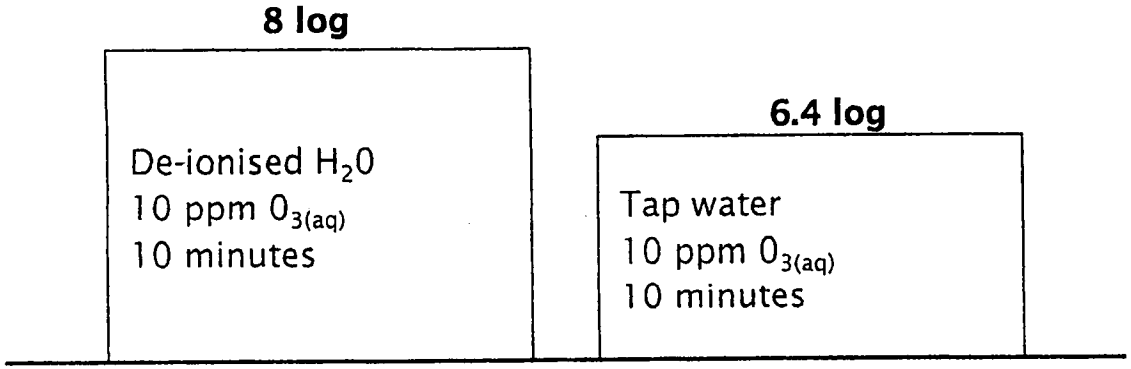
Test method:

- draining / drying period of 10 minutes before sampling
- flushed with 10-20mls of sterile water and collecting the washings and culturing the surviving organisms

Current developments: de-ionised vs. tap water

Extensive test work undertaken using de-ionised water and a log 8.5 "spike"

- ***Reduced particulate as de-ionised water***
- ***Reduced ozone demand (ie the free radicals generated from the ozone are not "used" by interacting with ions)***
- ***Greater biocidal efficacy / quicker bio-deactivation***



- ***Current development programme is focussing on the use of tap water due to commercial / practical considerations***

Current developments: use of surfactants

We investigated the potential advantages of using a surfactant for the following reasons:

- ability to use a lower concentration of aqueous ozone
  - quicker generation of active biocide
  - lesser risk of material compatibility issues
- ability to use tap water (cf. de-ionised water)

SURFACTANTS

- promotes the migration into suspension of particulates - including bioburden - ie reduces the amount of bioburden sticking to the surface of the endoscope
- biocidal efficacy of aqueous ozone is improved when bioburden is in suspension due to 3D exposure (ie the surface area of the bioburden exposed to the biocide is increased (cf. surface only (2D) exposure))
- R&D work is currently focussing on the use of a conventional cationic and anionic surfactant

Specifics of the endoscope washer disinfector

$O_{3(aq)}$ biocide	Validation features
▪ biocide generated in-situ	▪ validated software using a PLC
▪ *de facto* bacteria-free water final rinse	▪ endoscope identification using electronic tagging
▪ low level disinfection (ie log 6.5 kill) or	▪ operator identification
▪ high level disinfection (ie log 8 kill)	▪ batch identification
▪ no operator exposure issues (cf. glutaraldehyde)	▪ monitoring of the concentration of the biocide
▪ "single shot" process (ie biocide not re-used) - NB UK concerns re. prions	▪ data logging
▪ no discharge to drain problems	▪ traceability
	▪ remote diagnostics
	▪ instrumentation under development to validate the efficacy of the disinfection process

➡ ***This aqueous ozone biocide and validation technology should have applications for other re-usable medical devices which cannot be steam sterilised***

➡ ***BIOQUELL Medical is evaluating the relative advantages / disadvantages of marketing its endoscope washer as a high level disinfectant (ie log 8 kill) or a low level disinfectant (ie log 6 kill)***

Ability to use tap water (cf. de-ionised water)

Biocidal efficacy trials against other test species

- *bacillus subtilis* (spore forming)
- *mycobacterium terrae* (spore forming)
- *candida albicans* (pathogenic yeast)

Application of technology for use with other re-usable / quasi disposable medical devices

Application of technology to reduce hospital acquired antibiotic-resistant infection (eg MRSA, VRE)

Development of instrumentation to provide validation data to support the bio-deactivation efficacy of the disinfection cycle

Application of technology for clinical purposes

CLAIMS:

1. A method of cleaning medical equipment comprising the steps of flowing filtered water over surfaces of the equipment to be cleaned for a predetermined time followed by flowing ozonated water containing a predetermined concentration of ozone over said surfaces of the equipment for a predetermined time to disinfect the surfaces.

2. A method as claimed in claim 1, wherein the ozonated water is de-ionized prior to ozonating to the predetermined concentration.

3. A method as claimed in claim 2, wherein the de-ionized water is obtained from a supply of de-ionized water.

4. A method as claimed in claim 2, wherein the water is de-ionized by ozonating the water to remove free ions in the water following which ozone is added to the predetermined concentration.

5. A method as claimed in any of the preceding claims, wherein a surfactant is added to the ozonated water and the predetermined concentration of the water is reduced to a selected lower level.

6. A method as claimed in any of the preceding claims, wherein the flow of filtered water is obtained from tap water.

7. A method as claimed in any of the preceding claims, wherein the medical equipment has internal throughways and external surfaces to be cleaned wherein said filtered water and ozonated water are caused to flow through the internal surfaces and are

flowed or sprayed on the external surfaces to disinfect the external surfaces.

8. An apparatus for cleaning medical equipment comprising a supply of filtered water, a supply of ozonated water containing a predetermined concentration of water and means for delivering first a flow of filtered water over the surfaces of the equipment to be cleaned for a predetermined time followed by a flow of ozonated water over said surfaces for a predetermined time to disinfect the surfaces.

9. An apparatus as claimed in claim 8 where means are provided for de-ionizing the ozonated water prior to ozonating the water to said predetermined concentration.

10. An apparatus as claimed in claim 9, wherein means are provided for supplying ozone to the water to de-ionize the water prior to adding ozone to ozonate the water to said predetermined concentration.

11. An apparatus as claimed in any of claims 8 to 10, wherein means are provided for adding a surfactant to the supply of ozonated water and said means for ozonating the water are arranged to ozonate the water to a selected lower level.

12. An apparatus as claimed in any of claims 8 to 11, wherein means are provided for supplying tap water for use in the cleaning process and means are provided for filtering the tap water to provide said supply of filtered water.

13. An apparatus as claimed in any of claims 8 to 12, wherein said means for delivering said filtered water

and said ozonated water to the medical equipment comprises means for delivering said filtered water and said ozonated water to both internal and external surfaces of the equipment.

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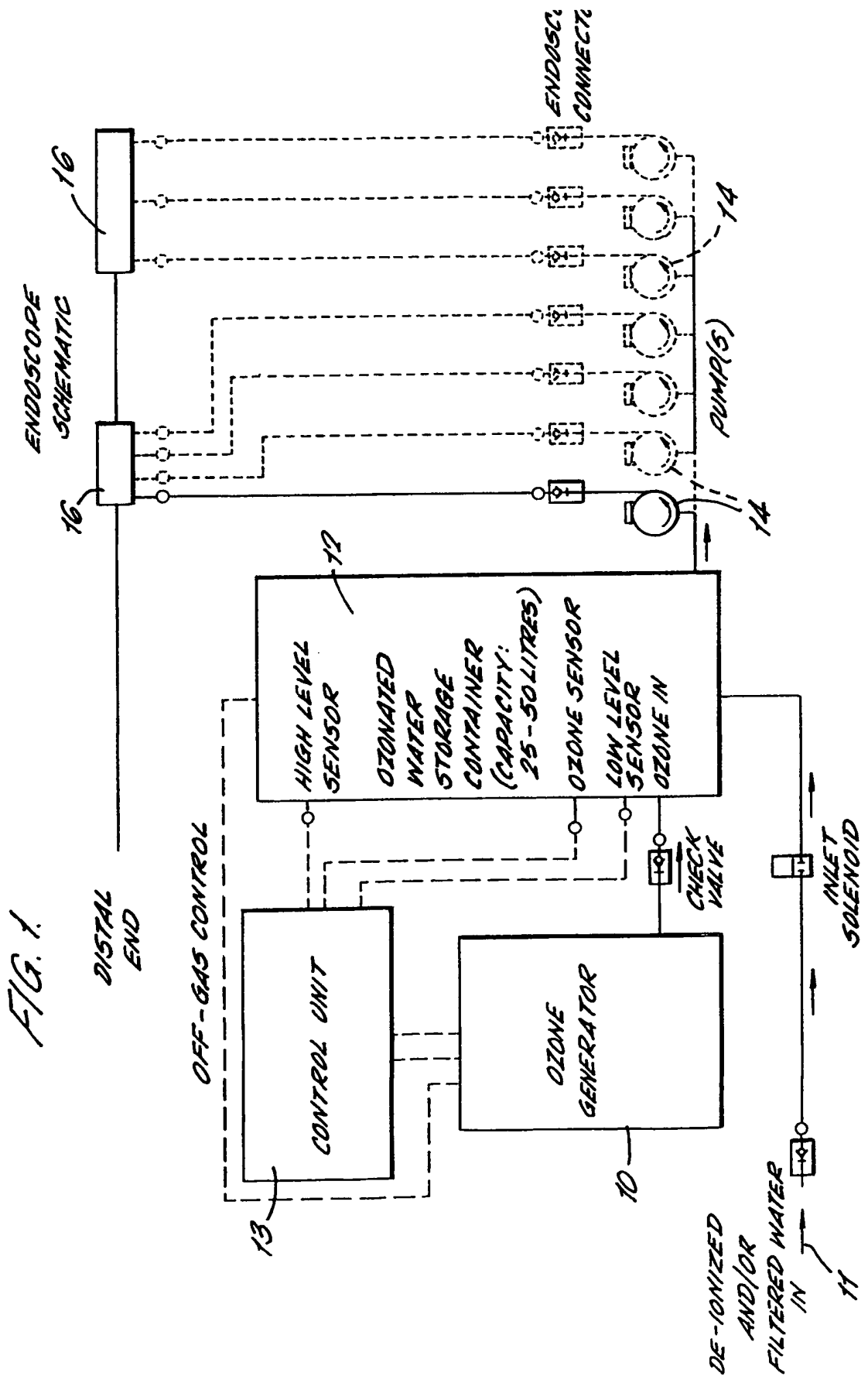

ENDOSCOPE SCHEMATIC
16
16
ENDOSCOPE CONNECTOR
14
PUMP(S)
14
12
HIGH LEVEL SENSOR
OZONATED WATER STORAGE CONTAINER (CAPACITY: 25-50 LITRES)
OZONE SENSOR
LOW LEVEL SENSOR
OZONE IN
CHECK VALVE
INLET SOLENOID
DISTAL END
OFF-GAS CONTROL
CONTROL UNIT
OZONE GENERATOR
13
10
DE-IONIZED AND/OR FILTERED WATER IN
11

FIG. 1.

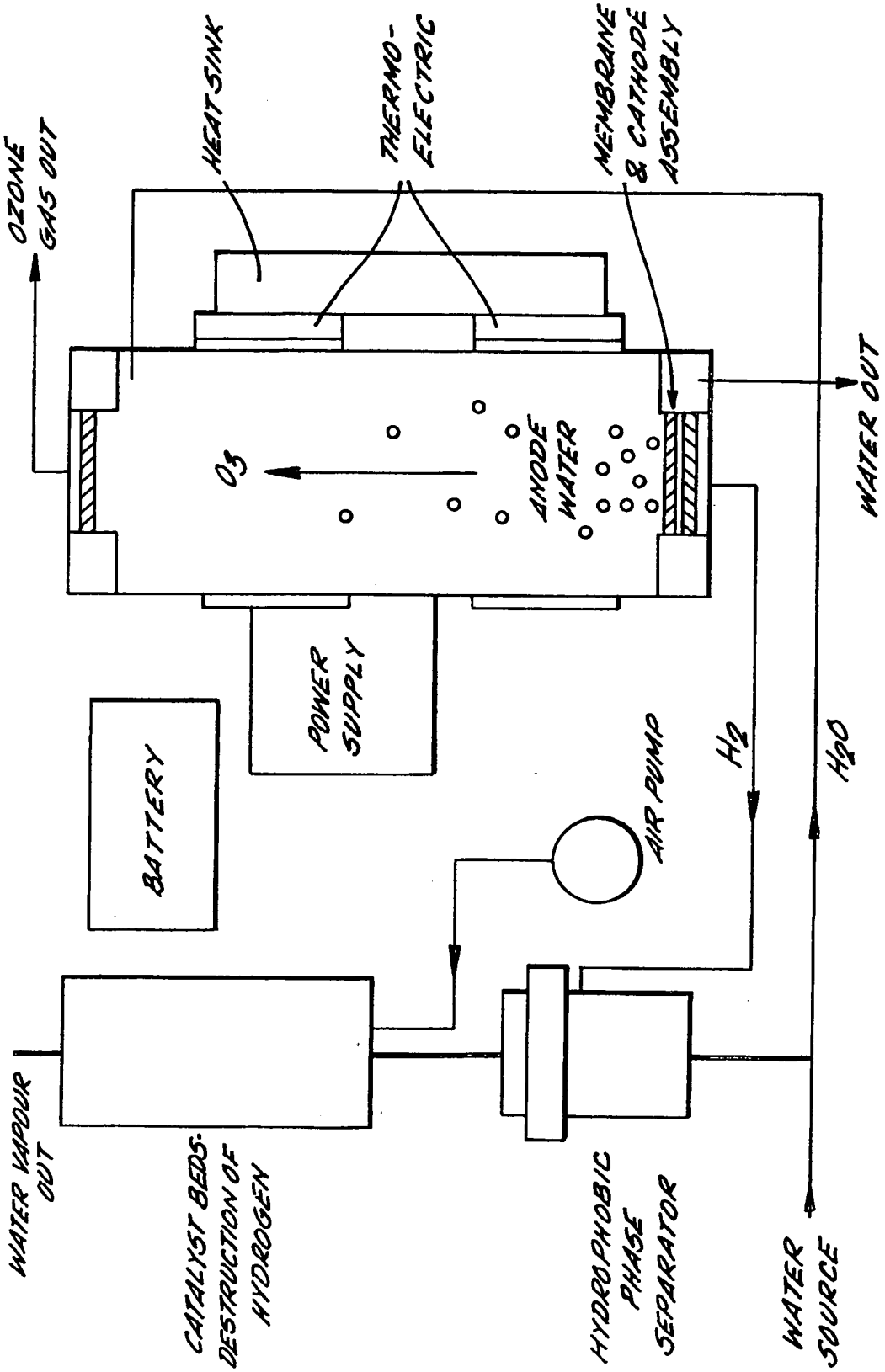


FIG. 2.
PEM OZONE GENERATION SYSTEM

FIG. 3.

SCHEMATIC DIAGRAM OF THE PEM CELL

WATER IS OXIDISED TO FORM O_2/O_3 - PROTONS (H^+) ALSO FORMED

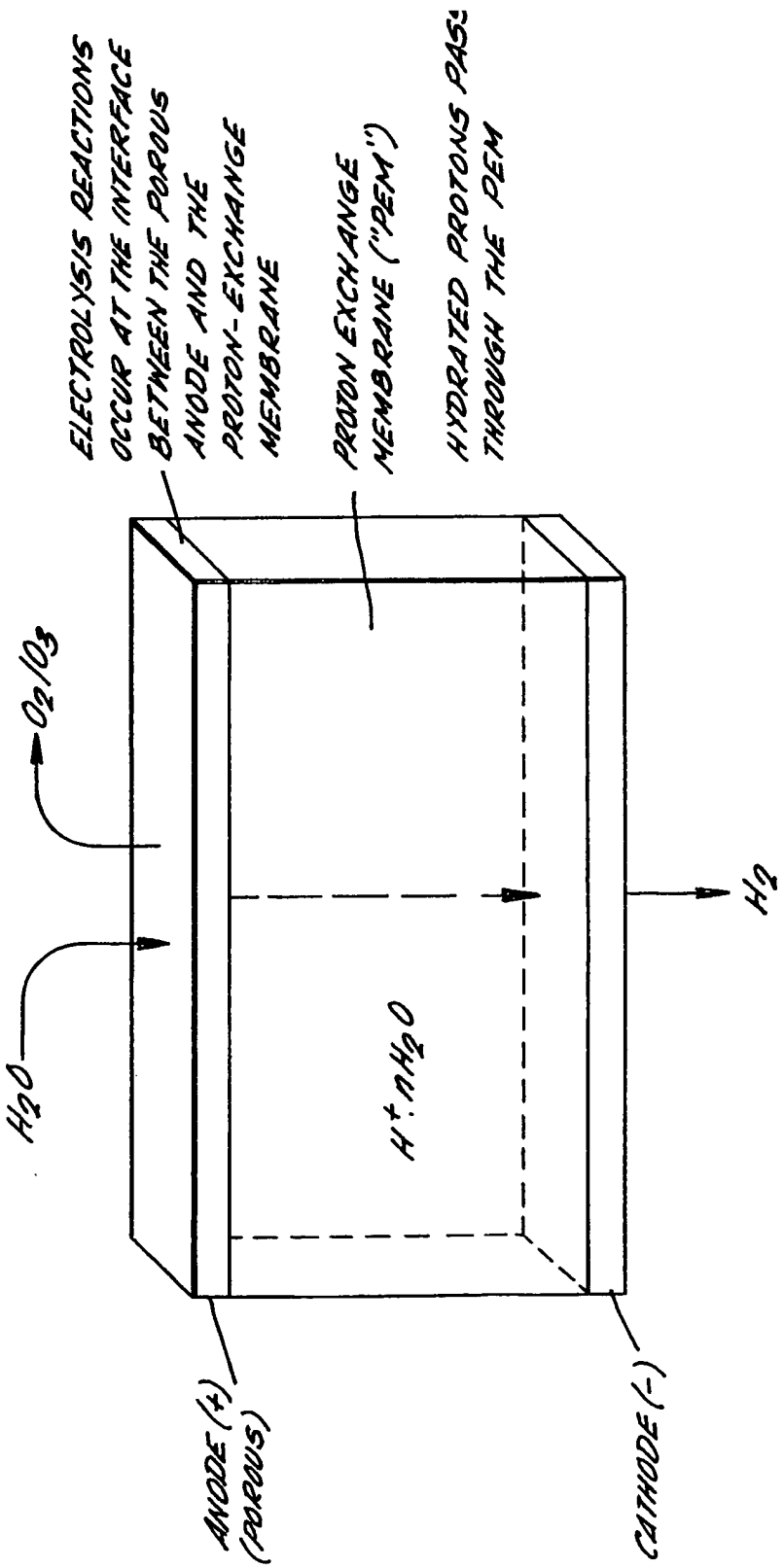
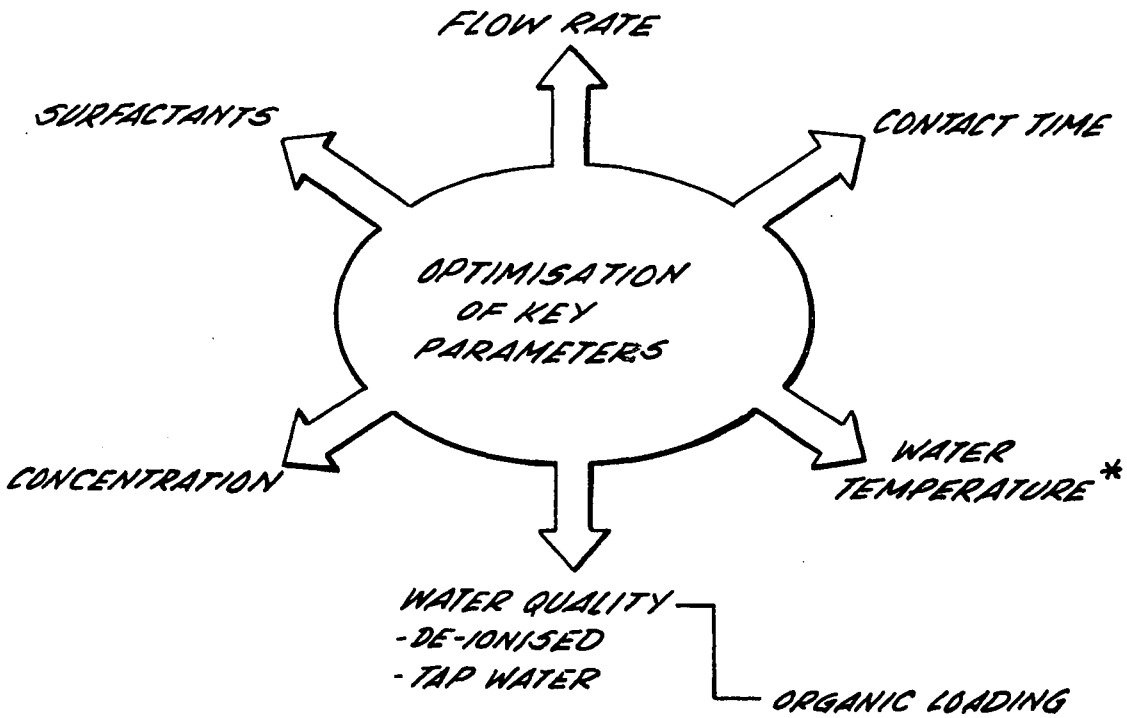


FIG. 4.

ISSUES AFFECTING BIOCIDAL EFFICACY OF AQUEOUS OZONE



⇨ OPTIMISATION HAS TAKEN C. 2 YEARS

* THE SOLUBILITY OF OZONE INCREASES WITH DECREASING WATER TEMPERATURE - BUT THE BIOCIDAL EFFICACY OF AQUEOUS OZONE DECREASES WITH DECREASING WATER TEMPERATURE DUE TO A REDUCED DEACTIVATION RATE (ie THE KILL KINETICS ARE ADVERSELY AFFECTED BY LOWER WATER TEMPERATURE)

FIG. 5.

AQUEOUS OZONE DEACTIVATION DATA FROM THE - OPTIMISATION PROGRAMME

5 MINUTES DE-IONISED/FILTERED TAP WATER
+ 10 MINUTES OZONATED WATER (LOG 9 LOADING)

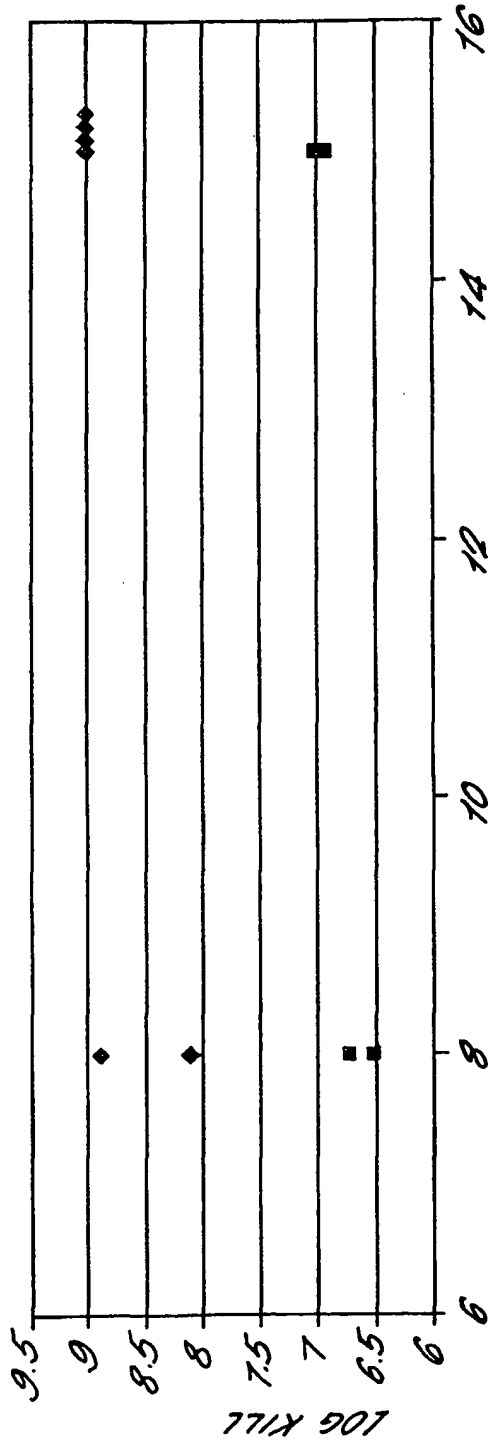


FIG. 6.

SUPER OXIDISED WATER - OPTIMISATION PROGRAMME

5 MINUTES DE-IONISED/FILTERED TAP WATER
+6 MINUTES OZONATED WATER (LOG 9 LOADING)

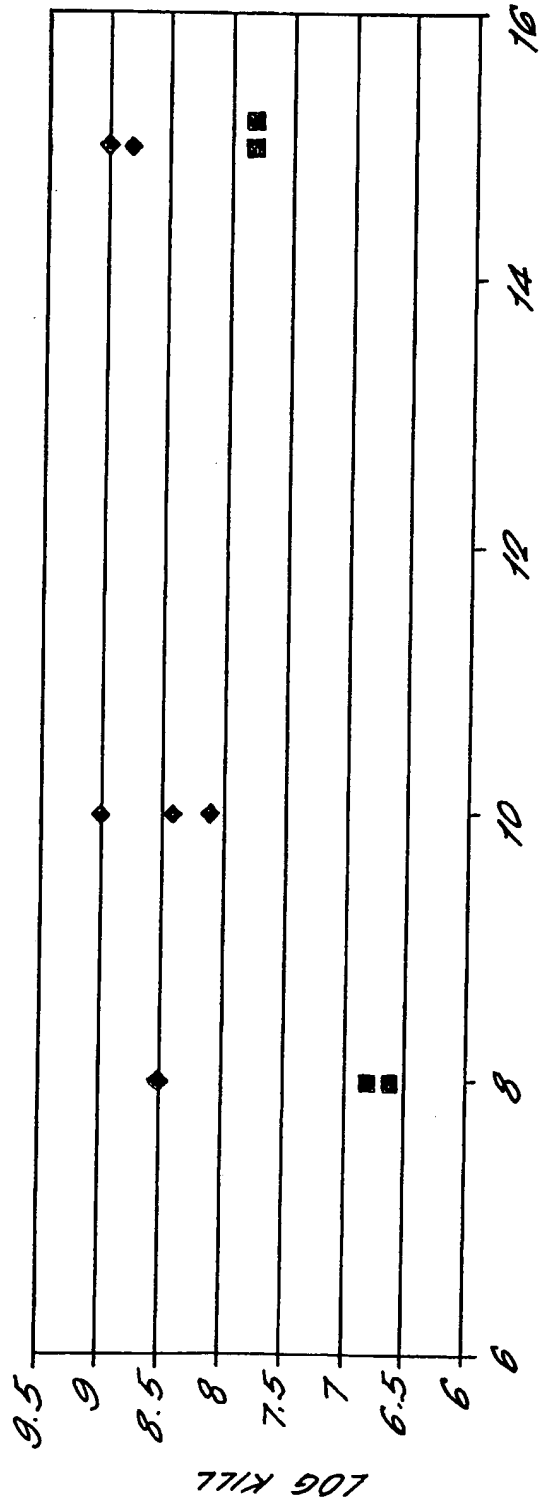


FIG. 7.

SUPER OXIDISED WATER - OPTIMISATION PROGRAMME

10 MINUTES DE-IONISED/FILTERED TAP WATER
+10 MINUTES OZONATED WATER (LOG 9 LOADING)

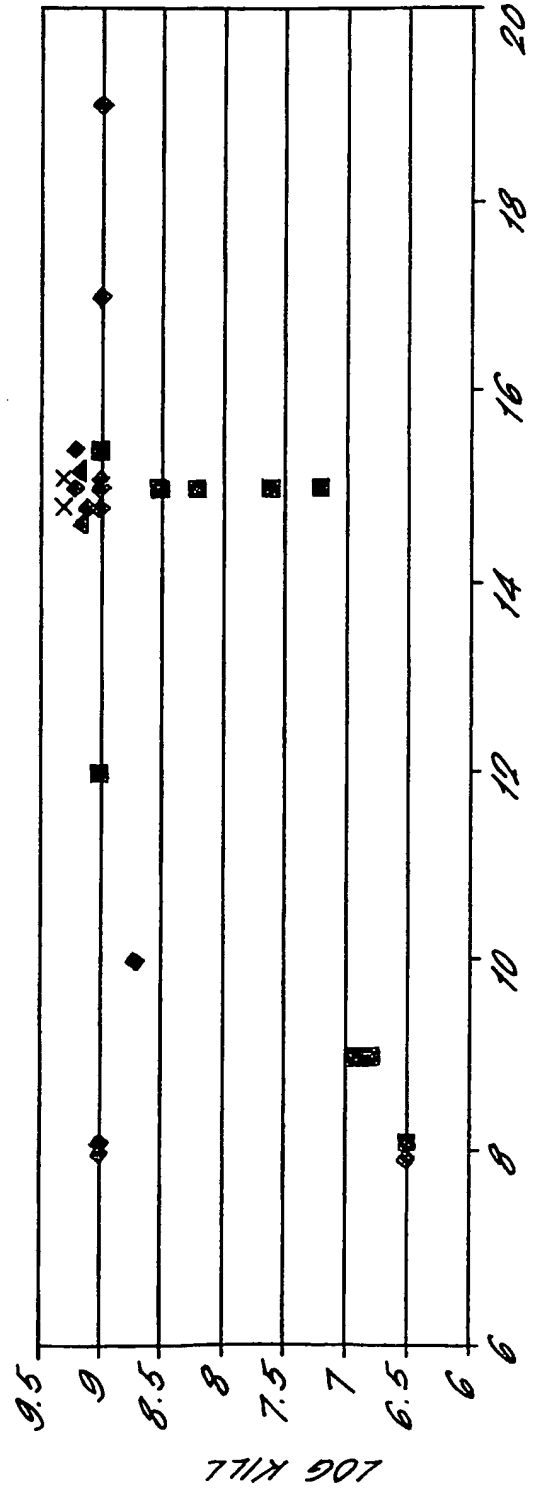


FIG. 8.

SUPER OXIDISED WATER - OPTIMISATION PROGRAMME

10 MINUTES DE-IONISED/FILTERED TAP WATER
+ 6 MINUTES OZONATED WATER (LOG 9 LOADING)

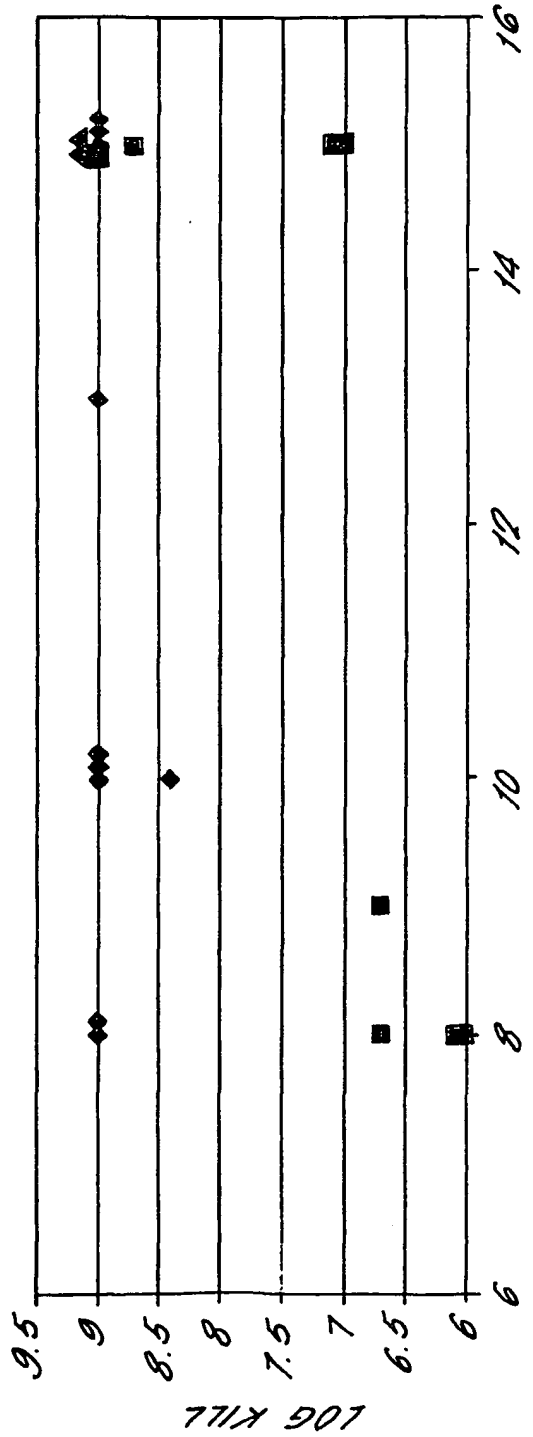
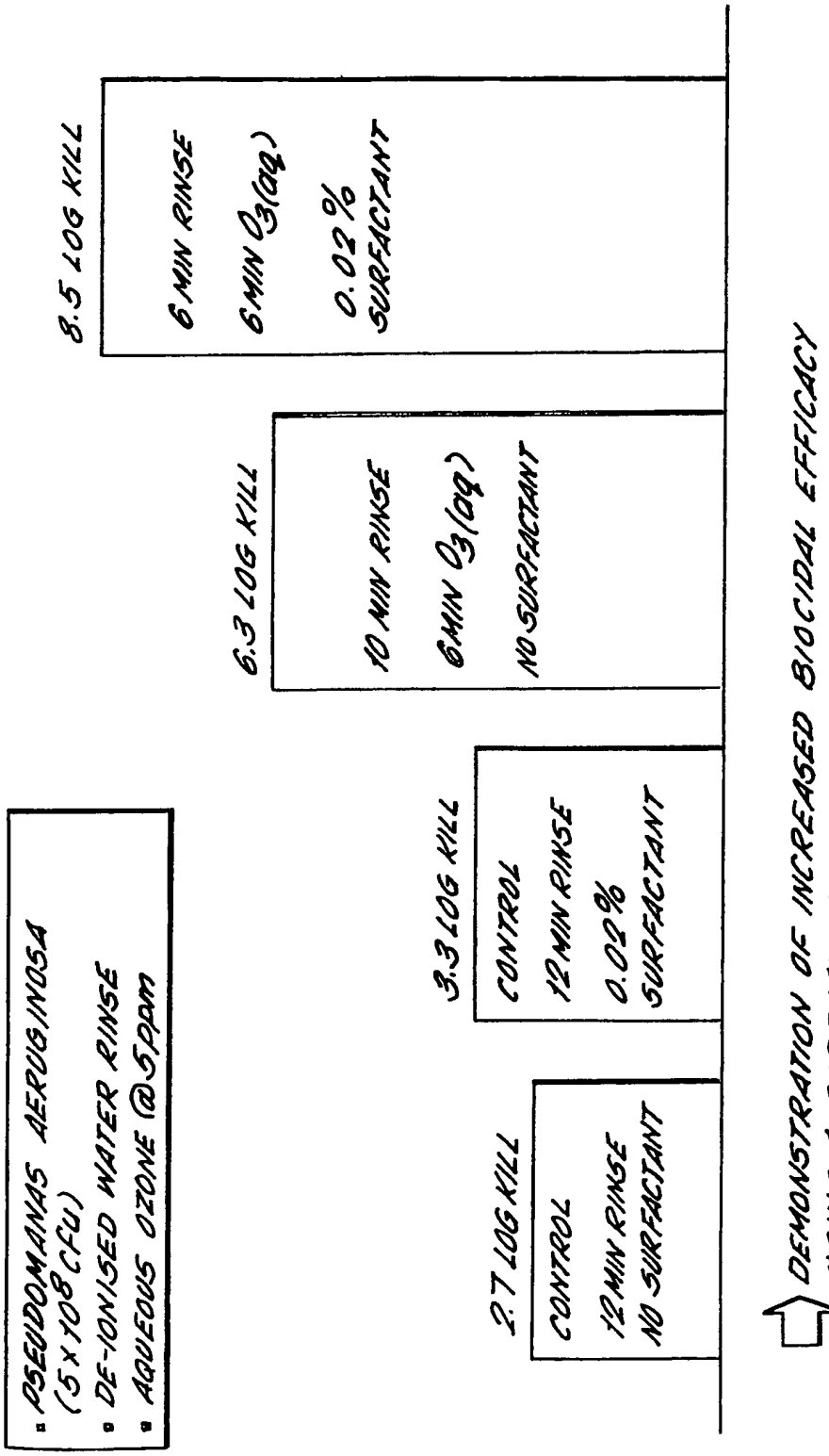


FIG. 9.

INCREASED EFFICACY OF AQUEOUS OZONE USING A SURFACTANT



INTERNATIONAL SEARCH REPORT

In pplication No
PCT/GB 01/04621

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L2/20 A61B1/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61L A61B C11D A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	US 5 897 832 A (PORTER BROOKS S) 27 April 1999 (1999-04-27) column 1, line 60 - line 67 column 3, line 63 -column 4, line 24 --- -/--	1-4, 6-10,12, 13

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
11 March 2002	21/03/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Menidjel, R

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INTERNATIONAL SEARCH REPORT

International application No
PCT/GB 01/04621

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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P,X	EP 1 116 491 A (NISSHO KK) 18 July 2001 (2001-07-18) column 4, line 40 - line 47 column 8, line 15 - line 23 column 6, line 52 -column 7, line 6 table 1	1-4, 6-10,12, 13

INTERNATIONAL SEARCH REPORT

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